PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/IB2004/004311	International filing date *(day/month/year)* 02.12.2004
Priority date *(day/month/year)* 02.12.2003	
International Patent Classification (IPC) or both national classification and IPC C07F9/06, A61K31/66, A61K39/39, A61P35/00, A61P31/00, A61P37/00	
Applicant INNATE PHARMA	

1. This opinion contains indications relating to the following items:

   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☒ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

   If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

   If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

   For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Richter, H Telephone No. +49 89 2399-8539

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2004/004311

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 16, partly 1-8

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 16, partly 1-8 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 16, partly 1-8

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2004/004311

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 9-15,17, partly: 1-8

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	12-15,17
	No:	Claims	1,9,11
Inventive step (IS)	Yes:	Claims	12-15,19,20
	No:	Claims	15,17
Industrial applicability (IA)	Yes:	Claims	1-15,17, 20
	No:	Claims	19

2. Citations and explanations

   see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III.

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of claim 1. So many documents were retrieved that it is impossible to determine which parts of the claim may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim is impossible. Consequently, the search has been restricted to compounds of formula (I) which are disclosed in the prior art (except D1, D17, D18) in connection with a biological activity or therapeutic use. Hence, the search was incomplete for claims 1 - 8.

Accordingly, no opinion with respect to inventive step of claim 1 and no opinion with respect to novelty and inventive step can be given for claims 2-8.

Re Item IV.

This Authority considers that there are 3 inventions covered by the claims.

The separate inventions 1-3 are shown in the search report.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

1. Claims for products defined in terms of processes for their preparation ("product-by-process" claims) are admissible only if - apart from any other conditions the products themselves fulfil the requirements for patentability, i.e. in particular if they are new and involve an inventive step.

"product-by-process" claims in general have to be interpreted in an absolute sense, ie independently of the process. Therefore, if the novelty of a "product-by-process" claim is at issue, novelty has to be examined and assessed independently of the potential novelty of the process.

As a consequence thereof inventions 1 and 3 are not so linked as to form a single general inventive concept (Rule 13.1 PCT).

2. Owing to its unclarity (see item VIII) the feature "γδ-T cell inhibitor" cannot be used as a feature which is able to link the inventions together.

3. Also, no connection can be seen between the preparation method according to invention 2 which does not aim at the preparation of a compound according to one of inventions 1 or 3.

Re Item V.

Reference is made to the following documents:

D1: XP 002329669
D2: XP 002329670
D3: XP 002329671
D4: XP 002329672
D5: XP 002329673
D6: XP 002329674
D7: XP 002329675
D8: XP 002329676
D9: DE-A-19815864
D9a: US-A-6627416
D10: XP 002329677
D11: WO-A-0018967
D12: WO-A-0036152
D13: XP 002329678
D14: XP 002329679
D15: XP 002329680
D16: WO-A-97/21452
D17: XP 002329874
D18: XP 002329875
D19: XP 001206357

Claims 1, 9, 11 lack novelty over D1-D19; see the search report for the exact details. Inter alia D9 and D9a describe pharmaceutical compositions containing a compound of formula (I). Further anticipating compounds can be found in the ampersand (&) documents.

No opinion can be given in regard of inventive step for claims 1-8 due to the unclarity of the feature "γδ-T cell inhibitor" (see item VIII).

None of the compounds of formula (I) has been mentioned in the prior art in connection with "activation of gamma,delta-T-cells"; "solid tumor" or "vaccine" or a similar term. Claims 12-14, 19, 20, therefore, seem to involve inventive merit.

None of the prior art documents describes a process according to claim 15.
D19 describes only step a. Hence, claim 15 is novel. Addition of steps b and c however cannot be considered inventive as being a standard chemical reaction (re-esterification). Hence, claims 15 and 17 seem to lack inventive merit.

Re Item VII.

If the applicants wish to incorporate the documents mentioned inter alia at pages 20 and 22 the disclosure thereof should be included expressis verbis in the description or the partial phrase "incorporated by reference" should be deleted.

Re Item VIII.

Claim 1 is directed to a chemical substance of formula (I) which is further limited by a functional feature "γδ-T cell inhibitor". This functional feature is not of the nature that a skilled person can easily decide from the structure of a compound whether it has the wanted activity or not. Claim 1, therefore, lacks clarity on account of the functional feature. Consequently, the functional feature has been ignored in the examination and search of the claims.

Medical applications of compounds of formula (I) are already disclosed in the prior art; see

item V, above. Claim 1 should, therefore, be cast as a second medical use claim.

Claim 16 X = NH2 is in contradiction to claim 15 where X means halide.